

## REMARKS

Applicants respectfully request entry of the amendments and remarks presented herein. Claims 52-59 stand rejected. Claims 61-66, 78, 90, and 102 are cancelled herein without prejudice. Claim 52 is amended to recite that each primer pair, in the presence of mammalian genomic DNA and under polymerase chain reaction (PCR) conditions, produces a nucleic acid product corresponding to a region of SEQ ID NO:1, wherein the product is 30 to 1650 nucleotides in length. Claim 58 is amended to recite that the first and second primers, in the presence of mammalian genomic DNA and under PCR conditions, produce a nucleic acid product corresponding to a region of SEQ ID NO:1, wherein the product is 30 to 1650 nucleotides in length. Claims 53 and 59 are amended to recite that the nucleic acid product comprises a nucleotide sequence variant relative to the corresponding region of SEQ ID NO:1. Support for these amendments can be found in Applicants' specification at, for example, page 13, lines 9-25.

New claims 105-108 have been added. Claims 105 and 107 depend from claims 53 and 59, respectively, and recite that the nucleotide sequence variant relative to the corresponding region of SEQ ID NO:1 is at position 107, 5895, 9689, or 664 of SEQ ID NO:1. Claims 106 and 108 depend from claims 105 and 107, respectively, and recite that the nucleotide sequence variant is a thymine substitution for cytosine at position 107 of SEQ ID NO:1, an adenine inserted at position 5895 of SEQ ID NO:1, an adenine deletion from position 9689 of SEQ ID NO:1, or a guanine substitution for adenine at position 664 of SEQ ID NO:1. Support for claims 105-108 can be found in Applicants' specification at, for example, page 63, lines 1-2, in Table 6 at page 54, and in Table 10 at pages 69-72. Thus, no new matter has been added.

In light of this amendment and the following remarks, Applicants respectfully request reconsideration and allowance of claims 52-59 and 105-108.

### Claim Objections

The Examiner objected to claims 52-59, because claims 52 and 58 recite the acronym ARPKD. The present claims do not include the acronym ARPKD. Thus, this objection is moot.

Rejections under 35 U.S.C. § 112

The Examiner rejected claims 52-59 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserted that the genus of nucleic acids encompassed by “an ARPKD nucleic acid molecule” is very large, and “includes hundreds of thousands of members each of which inherently possesses different structural and functional properties.” The Examiner further alleged that the specification does not disclose any ARPKD nucleic acids except *PKHD1* nucleic acids and does not satisfy the requirement to disclose a representative number of species, and that Applicants thus did not have possession of the claimed invention at the time of filing.

To further prosecution, Applicants have amended the claims to recite that the primer pairs, in the presence of mammalian genomic DNA and under polymerase chain reaction conditions, produce a nucleic acid product corresponding to a region of SEQ ID NO:1. Applicants’ specification fully describes the present claims. This is particularly true given that the specification sets forth the nucleic acid sequence of SEQ ID NO:1, and also provides a plurality of primer sequences that can be used to amplify portions of SEQ ID NO:1. *See*, for example, Table 5 at pages 51-53 of Applicants’ specification. Thus, a person of skill in the art, reading the specification at the time Applicants filed, would have appreciated that Applicants invented and were in possession of the claimed subject matter. As such, the written description requirement is satisfied.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 52-59 under 35 U.S.C. § 112.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 52-59 under 35 U.S.C. § 102(b) as allegedly being anticipated by the Park et al. reference (*Genomics* (1999) 57:249-255). The Examiner alleged that the Park et al. reference teaches a composition comprising a plurality of primer pairs, wherein each primer is 10-50 nucleotides in length, and wherein each primer pair, in the

presence of mammalian genomic DNA and under PCR conditions, produces a nucleic acid product corresponding to a region of an ARPKD nucleic acid molecule that is 30-1650 nucleotides in length.

Applicants respectfully disagree. As discussed above, the claims as amended herein recite that each primer pair, in the presence of mammalian genomic DNA and under PCR conditions, produces a nucleic acid product corresponding to a region of SEQ ID NO:1. The Park et al. reference does not anticipate the present claims. The primer sequences set forth in the Park et al. reference are described as falling throughout about a megabase of genomic nucleotide sequence. None of the primer sequences, however, are found within present SEQ ID NO:1, which is the cDNA sequence for *PKHD1*. Further, the Park et al. reference does not disclose the nucleotide sequences that were amplified or sequenced using the primers. To determine whether any of the Park et al. primers could be used to produce a nucleic acid product corresponding to a portion of SEQ ID NO:1, the undersigned agent used the EditSeq™ 5.0 program from DNASTAR Inc. to search for the Park et al. primer sequences within the human *PKHD1* gene sequence set forth in GenBank Accession No. NC\_000006. Forward and reverse complement sequences were searched for each primer, and if an entire primer sequence was not found within the gene sequence, an 8 to 10 nucleotide fragment from the center of the primer was searched. As indicated in the table below, ten of the primer pairs, plus one additional primer, were localized within the *PKHD1* gene sequence. Since these pairs are located only within introns, however, and are not positioned on either side of any exons, they would not be useful to amplify a region of SEQ ID NO:1. None of the remaining primers (i.e., those not listed in the table) were located within the genomic *PKHD1* sequence, despite the fact that fragments of the primers were searched. Thus, given the above, the Park et al. reference does not set forth a plurality of primer pairs that, in the presence of mammalian genomic DNA and under PCR conditions, each produces a nucleic acid product corresponding to a region of SEQ ID NO:1. As such, the present claims are novel over the Park et al. reference.

STS	Primer sequence	PKHD1 gene positions	Location
P357H1(T7)	CTTCTCCCTACACTGCCAC*	249732-249751	Intron 51
	GAATGACACCTTGACTGGT	249573-249592	Intron 51
P357H1(SP6)	CATCTAGATTGTCGTAACC	111038-111058	Intron 36
	ATGACACAGCATGGATAAAC*	111273-111293	Intron 36
B442L12(SP6)	AGAAACATCAACATTCTGGA*	403569-403589	Intron 58
	ATAGAAACACACCGCTCAGT	403476-403495	Intron 58
B449A13(T7)	CTATATTATGGCACTTGGC †	326462-326480	Intron 56
	AGAAGAGAGTTGGAGGGTC * †	326597-326616	Intron 56
P677J24(T7)	CCCATGAACTCTCTCTA*	118962-118981	Intron 36
	CTAGACTCAGCCTTGTGAAA	118795-118815	Intron 36
P742N16(T7)	ACCATTCTTTAACCAACCCC	335459-335478	Intron 61
	TGTAAAGAACTGGCCTCTGT*	335582-335601	Intron 61
B794E17(T7)	TGGTTATGACACTCCTGACA†	141383-141402	Intron 37
	TATAGACATGGGCTTGTCC* †	141540-141558	Intron 37
B857N11(T7)	TGCTTTAAAATTCTGGAAGG	64286-64305	Intron 33
	AGTTTCCTCTCCACTTAGGC*	64512-64531	Intron 33
B935B23(T7)	AAGTGTCTCCAGTATTGTGCT*	23284-23303	Intron 13
	TTAGCAAGGTGGAGAGTAG†	23074-23094	Intron 13
B989J7(T7)	GATGAGCTGTCTCCATGAG*	40425-40444	Intron 23
	AGGACCTTCTGGGTGCG**	40257-40274	Intron 23
P615K15(SP6)	CAAAATTCAACAAACATTCA* †	188153-188172	Intron 44
	GTTCATGAAACCAAGTTTC	N/L	N/L

\* - Reverse complement matched to *PKHD1* gene sequence.

† - Sequence matched to *PKHD1* gene sequence with one or more mutations.

N/L - Not localized within *PKHD1* gene sequence.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 52-59 under 35 U.S.C. § 102(b).

The Examiner rejected claims 52-59 under 35 U.S.C. § 102(b) as allegedly being anticipated by the Onuchic et al. reference (*Mammalian Genome* (1995) 6:805-808). The Examiner asserted that the Onuchic et al. reference teaches a composition comprising a plurality of primer pairs, wherein each primer is 10-50 nucleotides in length, and wherein each primer pair, in the presence of mammalian genomic DNA and under PCR conditions, produces a nucleic

acid product corresponding to a region of an ARPKD nucleic acid molecule that is 30-1650 nucleotides in length.

Again, the present claims recite that each primer pair, in the presence of mammalian genomic DNA and under PCR conditions, produces a nucleic acid product corresponding to a region of SEQ ID NO:1. As noted in Applicants' specification, SEQ ID NO:1 is the nucleotide sequence of the wild-type human *PKHD1* coding region. *See*, page 9, lines 19-20. At no point does the Onuchic et al. reference disclose primers that can be used to produce a nucleic acid product corresponding to a region of *PKHD1*. Thus, the Onuchic et al. reference fails to anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 52-59 under 35 U.S.C. § 102(b).

#### CONCLUSION

Applicants submit that claims 52-59 and 105-108 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please charge \$230 for the Petition for Extension of Time fee, and apply any other charges or credits, to deposit account 06-1050.

Respectfully submitted,

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